Remarks/Arguments

Claims 2 and 15 are pending in the present case. In the non-final Office Action dated November 30, 2010, claims "1 and 15" stand rejected under 35 USC §112, second paragraph, as being indefinite for failing to point out particularly and claim distinctly the subject matter which applicants regards as the invention. Claims 2 and 15 also stand rejected under 35 USC §103(a) as being obvious over "DHINGRA *et al.* (WO 98/04551), TEICHER *et al.* (WO 02/02094 A2), HEATH *et al.* (US patent no. 5,545,636)".

Claim 2 has been amended in response to the rejection under 35 USC §112, second paragraph. Basis for the amendment can be found in the specification on page 8, line 3. Claim 15 has been also been amended to correct antecedent basis. Basis for the amendment can be found in Claim 1. Applicants hereby submit the following arguments and remarks for consideration in connection with the above-identified patent application.

Additionally, Applicants hereby submit a supplemental information disclosure statement citing two internal (non-published) reports. See page 5, lines 5-12 of Applicants' specification.

Although the vehicle for the administration of the test compounds was not identified in the xenograft studies in TEICHER, Applicants believe the compounds were delivered at doses of less than 10 mg/mL and the vehicle was saline.

Claim Rejections - 35 USC §112

The Examiner has rejected "Claims 1 and 15" under 35 U.S.C. §112, second paragraph, as being indefinite for failing to point out particularly and claim distinctly the subject matter which applicants regard as the invention.

Applicants believe that the Examiner meant Claims 2 and 15 and have amended Claim 2 to recite "A crystalline… " instead of "Crystalline…". Applicants believe this amendment obviates the Examiner's rejection and respectfully request entry of the amendment and withdrawal of the rejection.

Claim Rejections – 35 USC §103(a)

Claims 2 and 15 stand rejected under 35 USC §103(a) as being obvious over "DHINGRA, TEICHER, HEATH".

The Examiner alleges that "DHINGRA teaches the compounds and hydrochloride salts of the claimed compound" and "teaches crystallized mono hydrochloride salts of such and similar

compounds and method for making them. See example 7 on page 31". The Examiner further alleges that "[i]t would have been obvious to one skilled in the art at the time of invention was made to prepare the crystalline pharmaceutically acceptable salts such as monohydrochloride salts of known compound because the prior art DHINGRA teaches the crystallized monohydrocholrides [sic] TEICHER et al and HEATH teaches the crystalline forms of dihydrochloride and teaches that since it contains a basic moiety, it can also exist as pharmaceutically acceptable acid addition salts. Acids commonly employed to form such salts include inorganic acids such as hydrochloric acid (lines 13-32, page 8), so the monochloride [sic] salt would be fairly suggested thereby." Applicants assert that the Examiner has failed to make a prima facie case of obviousness in regards to "DHINGRA, TEICHER, HEATH".

First, the compounds disclosed in DHINGRA (both generic and specific disclosures) are structurally distinct from the presently claimed compound (e.g., the compounds of DHINGRA require at least one substituent on each of the phenyl rings of the bis indoles whereas the presently claimed compound is unsubstituted at those positions) As such, the Examiner's assertion that "DHINGRA teaches the compounds and hydrochloride salts of the claimed compound" and "teaches crystallized mono hydrochloride salts of such and similar compounds and method for making them. See example 7 on page 31" is factually incorrect.

Second, it is unclear whether the Examiner is rejecting Applicants' claims over DHINGRA, TEICHER, **and** HEATH separately and/or in some combination thereof since the rejection simply states "obvious over DHINGRA, TEICHER, HEATH" with no conjunction.

Applicants believe the Examiner meant the present invention would be obvious because DHINGRA teaches allegedly crystallized mono-hydrochlorides of allegedly structurally similar compounds, TEICHER teaches a crystalline **dihydrochloride** variant of the presently claimed compound, and TEICHER and HEATH teach that because the freebase of the presently claimed crystalline mono-hydrochloride salt contains a basic moiety, it can also exist as pharmaceutically acceptable acid addition salts.

Regardless, DHINGRA provides no motivation for one of ordinary skill in the art to select Example 7 therein over the freebase of any of the other compounds disclosed in DHINGRA. Mono-hydrochloride salts are not preferred in DHINGRA and Example 7 is not disclosed to have any beneficial properties over any of the numerous other freebase compounds disclosed therein. Furthermore, Example 7 is silent on crystallinity, and lyophilization is not a

technique normally used to "crystallize" materials but is instead used to make amorphous materials.

> While the Examiner also points to the section of DHINGRA which states,
>
> "The conversion of an acidic compound of formula I into a pharmaceutically acceptable salt can be carried out by treatment with a suitable base in a known manner. Suitable bases are those derived not only from inorganic bases, for example, sodium, potassium or calcium salts, but also from organic bases such as ethylenediamine, monoethanolamine or diethanolamine. The conversion of a basic compound of formula I into a acceptable salt can be carried out by treatment with a suitable acid in a known manner. Suitable salts are those derived not only from inorganic acids, for example, hydrochlorides, hydrobromides, phosphates or sulphates, but also from organic acids, for example, acetates, citrates, fumerates, tartarates, maleates, methanesulfphonates or p-toluensulphonates.
>
> The pyrroles of formula I and their pharmaceutically acceptable salts inhibit cellular processes, for example cell proliferation, and can be used in the treatment or control of inflammatory disorders such as arthritis, immune diseases, in conjunction with organ transplants and in oncology". (Citing "Lines 1-13 on page 13"...which are actually lines 1-15 on page 13)

the Examiner omits the preceding paragraph which states,

> "If desired, an acidic compound of formula I can be converted into a pharmaceutically acceptable salt with a base or a basic compound of formula I can be converted into a pharmaceutically acceptable salt with an acid."

DHINGRA thus provides absolutely no explanation of the circumstances under which the conversion of the freebase compounds disclosed therein to a pharmaceutically acceptable salt would be desired.

Furthermore, Applicants respectfully assert that the passage the Examiner relies on from DHINGRA adds NOTHING to what Applicants have already successfully addressed on appeal. The Board of Patent Appeals and Interferences found that similar passages in TEICHER and HEATH did not support a prima facie case of obviousness against the presently pending claims.

In conclusion, while DHINGRA does illustrate a method of making a hydrochloride salt of a bisindole maleimide structurally distinct from the presently claimed compound, it does not teach, suggest, or motivate one skilled in the art to make Applicants' crystalline mono-HCl salt.

Additionally, because the Examiner brings up nothing new regarding TEICHER and HEATH, and TEICHER and HEATH have already been successfully argued before The Board of Patent Appeals and Interferences, this rejection as it relates to TEICHER and HEATH, has already been obviated. Applicants respectfully request the removal of this rejection.

If the Examiner has any questions, or would like to discuss any matters in connection with this application, she is invited to contact the undersigned at (317) 277-3537.

Respectfully submitted,

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